Remarks

Claims 1-24, 55-81, 183-186, 191, 192 and 203-210 are pending.

Rejections under 35 USC § 103

Curtet and Duclos.

Claims 1-24, 55-81, 183-186, 191, 192 and 203-210 are rejected under 35 USC § 103 as being obvious over Curtet (US Patent No. 4,895,726) in view of Duclos (US Patent 5,776,495).

Applicants respectfully traverse the rejection because Curtet does not disclose or suggest the claimed suspensions and the processes using them. At column 2, lines 5-20, Curtet identifies a process of:

(i) mixing and co-micronizing fenofibrate and a solid surfactant;
(ii) adding lactose and starch to the mixture; and converting the whole to granules in the presence of water;
(iii) drying the granules until they contain no more than 1% water;
(iv) grading the granules;
(v) adding polyvinylpyrrolidone[1] and magnesium stearate to the graded granules; and
(vi) filling gelatin capsules with the mixture.

Curtet adds water to the mixture of fenofibrate and surfactant; dries the mixture; and subsequently adds polyvinylpyrrolidone.[2]

Curtet does not disclose or suggest a suspension of fenofibrate. Additionally, Curtet does not teach a solution of at least one polymer, and does not provide any motivation to produce a solution containing at least one polymer. This is acknowledged by the PTO[3] that:

> *"Curtet et al do not expressly state a fenofibrate suspension, but rather a composition [...]"*

The PTO then states that:

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[1] Curtet's working examples all use cross-linked polyvinylpyrrolidone.
[2] *Id.*
[3] Office Action at page 6, first paragraph.

> *"Curtet et al do not expressly state a fenofibrate suspension, but rather a composition, wherein co-micronized granules are contained in the presence of water. However, it is well known in the art to incorporate a medicament, such as fenofibrate in combination with water and a surfactant to form a suspension."*

The PTO contends that it is obvious for the skilled person to modify a solid composition into a liquid, aqueous, suspension comprising a surfactant. Claim 1, however, does not recite any surfactant (while claim 55 does).

Applicants respectfully submit that Curtet teaches away from a suspension. Indeed, Curtet states (e.g., abstract and claim 1):

> *"a composition containing a co-micronized mixture of particles of fenofibrate and a solid surfactant"* (emphasis added).

Curtet requires the surfactant to be in a solid form. The claimed invention requires the surfactant or the polymer to be in a solution, hence, in a dissolved form, which is very different from a solid form.

The claimed invention requires that the suspension be sprayed onto an inert carrier. The suspension is an intermediate product which is used in the manufacture of a final composition. *See* Specification at page 7, lines 19-21. The specific suspension, when used as spraying material, e.g., in a fluidized bed granulator, provides a final composition having an improved dissolution. The suspension itself is not used as a dosage form for the active ingredient, but as an intermediate in the manufacture of the final dosage form. It is irrelevant whether fenofibrate in a suspension would provide increased bioavailability[4], because the suspension is not administered to a patient. The solid dosage form obtained from the process using the suspension is administered to a patient.

The invention is drawn to a specific process for making a dosage form which may be a tablet or granulates in a capsule. The process of the invention uses a specific suspension in a spraying process, where the suspension containing the active ingredient is sprayed onto inert carriers. Curtet's process is far different because it uses wet granulation, and never uses a suspension. Water added in the Curtet process only serves granulation and will not allow a

solution of surfactant to be obtained. 8.9% of water based on the dry matter is used to granulate, excluding any solution of surfactant dissolved in water. Curtet does not disclose a suspension or a process using a suspension to form a fenofibrate composition.

Accordingly, Curtet does not render the claimed invention obvious.

Duclos does not cure the deficiencies of Curtet. Duclos discloses and claims a process for preparing a solid dispersion (e.g., claim 1 and the abstract). Duclos states that a surfactant can assist in improving dissolution of poorly water-soluble drugs. Duclos provides the same statements as Curtet. Both references teach the use of a surfactant. However, Duclos discloses the use of surfactant in a solid dispersion. At page 2, lines 20-22, Duclos states that the process comprises the step of dissolving an active ingredient in an organic solvent (which may further contain the surfactant). This solution of active ingredient in a solvent with a polymer and a surfactant is then subjected to the process of forming the co-precipitate by using dissolution-evaporation (e.g., column 3, lines 1-2). The resulting composition is suitable for administering an active ingredient as a solid composition.

Duclos states that an intermediate solution can be used to produce the co-precipitate. A solution is distinct and different from a suspension.

The term "suspension" is well known in the art and is defined, for example, as follows:

> (1): the state of a substance when its particles are mixed with but undissolved in a fluid or solid (2): a substance in this state (3): a system consisting of a solid dispersed in a solid, liquid, or gas usu. in particles of larger than colloidal size

Webster's New Collegiate Dictionary, G&C Merriam Company, page 1165 (1981).

The term "solution" is well known in the art and is defined, for example, as follows:

> "solution (1) Dissolution. The mixing of a solid, liquid, or gaseous substance (solute) with a liquid (the solvent), forming a homogeneous mixture from which the dissolved substance can be recovered by physical processes. (2) The homogeneous mixture formed by the operation of s[olution]."

Grant & Hackh's Chemical Dictionary, 5th Ed., McGraw-Hill, Inc., page 541 (1987).

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[4] Office action at page 5

Because the terms solution and suspension are different, the solution of active ingredient of Duclos is different than the suspension of active ingredient of the claimed invention. Duclos does not teach a suspension of micronized active ingredient, but a solution containing the active ingredient in a dissolved form. The invention is, in contrast, directed to a suspension of fenofibrate in a micronized form.

The skilled person would not "*incorporate a suspension of micronized fenofibrate as taught by Duclos et al within the fenofibrate composition of Curtet et al*" as is stated by the PTO. Duclos fails to disclose a suspension. Water added in the Curtet process only serves granulation and will not allow a solution of surfactant to be obtained. 8.9% of water based on the dry matter is used to granulate, excluding any solution of surfactant dissolved in water. Duclos teaches a process for the manufacture of a solid dosage form, using a solution of dissolved active ingredient.

Because none of the cited references disclose or teach a suspension, the claimed invention cannot be obvious over the prior art. None of the cited references disclose or teach the step of spraying a suspension onto inert carrier particles.

Contrary to what the PTO states, "*because Duclos teach micronization of medicaments in suitable form such as suspensions, can be beneficial in increasing the solubility of active components and thereby improving the kinetics of resorption and consequently, the bioavailabilty of active ingredients.*", Duclos fails to teach micronization. Duclos is only concerned with micronization at column 1, lines 24-37, in the section dedicated to the prior art. First, this statement is a very broad statement, and not based on references. Second, Duclos immediately criticized these existing possibilities. Thus, Duclos teaches away from using micronized active ingredient (with or without a surfactant). Duclos provides a technical approach which involves a dissolution step, whereby the micronization is necessarily lost (and is not recovered during the later stages of the process, including evaporation).

The claimed invention provides a process comprising the steps of (i) providing a suspension and (ii) spraying said suspension onto inert carriers. The Office Actions states at page 6, last sentence, that

"the expected result would be an improved process for obtaining a bioavailable fenofibrate suspension formulation, which can be administered once a day."

This, as was previously explained, is clearly not the invention. The suspension is not used itself as a final composition to be administered to a patient, but as an intermediate product in the process. The process as presently claimed is not a process for obtaining a suspension, but a process which will use the suspension to produce a fenofibrate composition. Consequently, the suspension does not exist in the final product obtained by the claimed process. Only the solid dosage form obtained by the claimed process is administered to a patient.

In view thereof, Applicants respectfully submit that the claimed invention is unobvious over Curtet in view of Duclos, and respectfully request that the rejection under 35 USC § 103 be withdrawn.

Curtet and Ikeda.

Claims 1-24, 55-81, 183-186, 191, 192 and 203-210 are rejected under 35 USC § 103 as being obvious over Curtet (US Patent No. 4,895,726) in view of Ikeda (US Patent 5,952,356).

Curtet has been analyzed above, the analysis of which is incorporated by reference herein in its entirety.

Ikeda does not cure the deficiencies of Curtet. Ikeda is directed to a specific combination of an antidiabetic, comprised of an insulin sensitivity enhancer, together with another antidiabetic having a different mode of action. Ikeda identifies eight other categories of drugs that have a different mode of action, including fibrates.[5] Ikeda then identifies fifteen different fibrate compounds, one of which is fenofibrate.[6] Ikeda states no preference for any fibrate compound. Ikeda does not provide any working or prophetic examples that use any type of fibrate or any of the fifteen different fibrate compounds identified therein. Ikeda is also completely alien to the issue of increasing the bioavailability of fenofibrate. For this reason only, the skilled person would not revert to Ikeda.

Suspensions are mentioned in a list of possible dosage forms. *See* Ikeda at col. 13, lines 51-58. The process for manufacturing liquid dosage forms is stated at column 14, lines 37-39,

[5] Ikeda at column 11, line 1.

referring back to the method of manufacturing injections. Injections are identified at column 14, lines 12-28. Again, no preference or emphasis is placed on suspensions. From a reading of Ikeda, the skilled person would not gain any specific knowledge about processes using suspensions, let alone processes using suspensions of the fibrate class of drugs, let alone processes using suspensions of fenofibrate (which is one of fifteen fibrates identified by Ikeda).

The skilled person would not contemplate reading Curtet and Ikeda together because they are concerned with two remote fields. Ikeda is non-analogous art. There is nothing in Ikeda remotely related to the claimed invention.

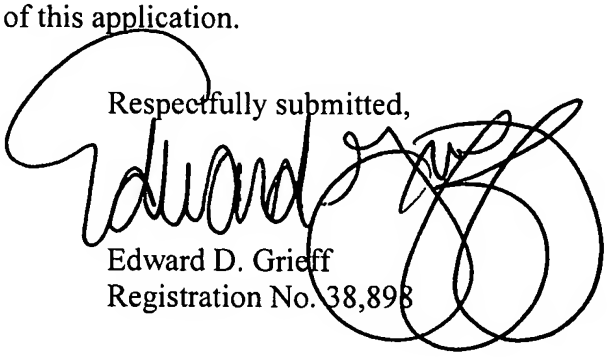
The claimed suspensions are not the dosage form to be administered to a patient, but an intermediate product used in the manufacture of a final dosage form. Neither Curtet nor Ikeda discloses or suggests the use of suspensions as intermediate products in the manufacture of final dosage forms, let alone the step of spraying the suspension onto inert carriers.

In view thereof, Applicants respectfully submit that the presently claimed invention is unobvious over Curtet in view of Ikeda, and respectfully request that the rejection under 35 USC § 103 be withdrawn.

Conclusion

An early and favorable reconsideration and allowance of claims 1-24, 55-81, 183-186, 191, 192 and 203-210 is respectfully requested. Examiner Sheikh is encouraged to contact the undersigned to expedite prosecution of this application.

Respectfully submitted,



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[6] Ikeda at column 12, lines 1-5.